

CLAIMS

What is claimed is:

5 1. A method for the detection of cancer, appraising the prognosis thereof, and/or risk therefor comprising the steps of:

- a) obtaining essentially non-malignant cells from an individual; and
- b) determining the coordination between alleles of one or more DNA loci in said cells.

10 2. A method according to claim 1 wherein the coordination is synchrony in replication timing.

15 3. A method according to claim 1 wherein the coordination is chromatin conformation.

 4. A method according to claim 1 wherein the coordination is methylation.

20 5. A method according to claim 4 wherein the coordination is hypermethylation and/or hypomethylation.

 6. A method according to claim 1 wherein the coordination is gene expression.

25 7. A method according to claim 1 wherein the coordination is fidelity of chromosome segregation.

30 8. A method according to claim 7 wherein chromosome segregation is expressed in losses and/or gains of chromosomes (aneuploidy).

9. A method according to claim 1 wherein the cells are subjected to a growth stimulus before step (b).

10. A method according to claim 1 wherein the cells are subjected to
5 chromatin and /or DNA modifiers before step (b).

11. A method according to claim 10 wherein the cells are subjected to chromatin and /or DNA modifiers selected from 5-azacytidine, Trichostatin A, Sodium Butirate, N-nitroso-n-methylurea.

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12. A method according to claim 1 wherein the cells are derived from a body tissue or body fluid.

13. A method of claim 12 wherein the body tissue is bone marrow.

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14. A method of claim 12 wherein the body fluid is selected from blood, amniotic fluid, urine, and saliva.

15. A method of claim 14, wherein the blood is peripheral blood.

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16. A method of claim 12 wherein the cells are lymphocytes.

17. A method of claim 15 wherein the cells are lymphocytes.

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18. A method of claim 15 wherein the locus or loci are non-coding DNA regions.

19. A method of claim 18 wherein the locus or loci are selected from satellited DNA arrays.

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20. A method of claim 19 wherein the locus or loci are centromere-associated.

21. A method of claim 1 wherein the locus or loci are expressed biallelically.

5 22. A method of claim 1 wherein the locus or loci are selected from tumor-associated genes.

23. A method of claim 10 wherein the locus or loci are selected from oncogenes, tumor suppressor genes, and transcription factors

10 24. A method according to claim 1 wherein the locus or loci are expressed monoallelically.

15 25. A method of claim 24 wherein the locus or loci are selected from imprinted loci, loci on the X-chromosome in female individuals and loci subjected to allelic exclusion.

26. A method of claim 25 wherein the imprinted locus is the Prader-Willi locus.

20 27. A method of claim 1 wherein the locus or loci are selected from among HER2, CMYC, TP53, RB1, D21S55, GABRB3, SNRPN, D15S10, D22S75 and DSTS WI-941. as well as alpha, II and III satellites for all chromosomes.

25 28. A method of claim 1 wherein a change in coordination is indicative of cancer, the prognosis of cancer, or the risk therefore, is detected.

30 29. A method of claim 28 wherein the change in synchrony is between about 3 and about 55%.

30. A method of claim 29 wherein the change in synchrony is an increase in asynchrony.

31. A method of claim 30 wherein the increase is between about 25
5 and about 30%.

32. A method of claim 29 wherein the change in synchrony is a decrease in asynchrony.

10 33. A method of claim 32 wherein the decrease is about 15%.

34. A method of claim 1 wherein synchrony is measured by fluorescence in situ hybridization, using a probe targeted to a bialelically expressed gene, in cells derived from peripheral blood, and wherein an
15 increase in asynchrony of about 15 to about 35% is indicative of cancer, the prognosis thereof, or risk therefor.

35. A method of claim 1 wherein synchrony is measured by fluorescence in situ hybridization, using a probe targeted to a monoallelically
20 expressed gene, in cells derived from peripheral blood, and wherein a decrease in asynchrony of about 10 to about 20% is indicative of cancer, the prognosis thereof, or risk therefor.

36. A method of claim 1 wherein synchrony is measured by fluorescence in situ hybridization, using a probe targeted to a non-coding
25 DNA entity, in cells derived from peripheral blood, and wherein a increase in asynchrony of about 15 to about 35% is indicative of cancer, the prognosis thereof, or risk therefor.

37. A method of identifying cancer, appraising the prognosis
30 thereof, or risk for the development thereof in a mammal, substantially as described and with particular reference to the examples and figures.

38. A method for detecting cancer and cancer risk by analyzing a pattern of behavior of an allele in relation to its counterpart from *ex vivo* cells whereby an altered pattern corresponds to the presence of cancer and/or a cancer risk.

39. A method according to claim 38 wherein said analyzing step is further defined as analyzing patterns of behavior selected from the group including replication, expression, levels of methylation, conformation, and acethylation of homologous DNA sequences.

40. The method according to claim 38, wherein said analyzing step is further defined as including methods from the group consisting of fluorescence *in situ* hybridization.

41. The method according to claim 38, further including the step of deriving peripheral blood cells.

42. The method according to claim 38, wherein said isolating step includes deriving cells from bodily fluids and tissues.

43. The method according to claim 38, wherein said analyzing step includes analyzing coding and/or noncoding sequences.

44. A method of determining a cancerous status of DNA sequences by:
assaying cells to determine the allelic pattern status of the DNA.

45. The method according to claim 44, wherein said assaying step includes performing a fluorescence *in situ* hybridization to determine the mode of allelic replication.

46. A diagnostic test for detecting cancer or the risk of cancer comprising:

allelic replication viewing means for viewing the pattern of behavior of at least one coding and/or noncoding;

5 a standardized table of replication patterns; and

analysis means for determining an altered pattern of behavior of DNA entity, whereby the altered pattern is diagnosed as a cancer characteristic.

10 47. The test according to claim 46, wherein said allelic replication viewing means is fluorescence *in situ* hybridization.

48. The test according to claim 46, wherein said analysis means is capable of analyzing replication patterns of the coding and/or noncoding DNA
15 entity selected from the group consisting essentially of expressed genes and unexpressed DNA entities responsible for the segregation of genetic material.

49. The test according to claim 46, wherein said test is used for detecting cancers selected from the group consisting essentially of solid and
20 humoral tumors.

50. A method for differentiating between different malignancies comprising the steps of:

subjecting sequences to allelic-specific characterization; and
25 analyzing replication status of the sequences to distinguish between malignancies

51. A method of detecting agents causing genomic destabilization associated with either changes in the pattern of behavior of an allele in
30 relation to its counterpart (allele-specific behavior) and/or losses and gains of chromosomes comprising the steps of:

applying an agent to isolated cells; and

analyzing coding and/or noncoding DNA status of the isolated cells whereby an altered pattern corresponds to genomic (genetic) destabilization.

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